

Potentially Inappropriate Medications in Geriatric Outpatients' Prescriptions in Yogyakarta: Patterns and Associated Factors

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ABSTRACT

We commonly found potentially inappropriate medications (PIMs) in the prescriptions of geriatric patients and widely assessed them using the Beers Criteria and the STOPP/START tool. In this study, we aimed to assess the patterns of PIMs in geriatric outpatients in Yogyakarta, Indonesia, and the factors related to their occurrence. We conducted this study at two teaching hospitals in Yogyakarta, Indonesia, using a retrospective observational design. The data source included medical records of the outpatients aged ≥ 60 years during August to October 2022. The 2019 AGS Beers® Criteria and the STOPP_INA tool, based on STOPP/START version 2, were used to evaluate PIMs from the prescriptions. We analyzed several predictors, including multimorbidity, polypharmacy, age, sex, health insurance, and working status, using logistic regression. This study identified 193 cases of PIMs in 135 patients (34.35%) out of the 393 subjects, with 67 cases according to the Beers Criteria and 141 cases according to STOPP_INA. We found that the most common drugs causing PIMs in geriatric patients were aspirin and benzodiazepines. Polypharmacy emerged as the strongest predictor of PIMs occurrence ($p < 0.05$). Polypharmacy significantly influenced the prevalence of PIMs in outpatient geriatric prescriptions. Therefore, there is a pressing need for vigilant monitoring and meticulous drug selection by healthcare providers when prescribing for the elderly population to mitigate the potential risks associated with PIMs.

Keywords: potentially inappropriate medication, multimorbidity, polypharmacy

INTRODUCTION

Potentially Inappropriate Medications (PIMs) are drugs that are more likely to cause an adverse drug reaction (ADR) than to help the patient when given to older people (Renom-Guiteras et al., 2015). The prevalence of PIMs among geriatric patients ranged from approximately 40–50% in some countries (Koçak et al., 2022; Chou et al., 2021; Alhawassi et al., 2019; Magalhães et al., 2019), with a study in Karawang District, Indonesia, revealing the occurrence of PIMs in 52.2% of geriatric patients (Abdulah et al., 2018). The use of PIMs is associated with increased

hospitalizations, emergency department (ED) visits, and more frequent physician consultations compared to non-PIM users. Consequently, these outcomes lead to higher mean healthcare expenditures, posing a significant economic burden to both patients and governments (Clark et al., 2020).

Several studies have identified factors associated with PIMs occurrences, including multimorbidity and polypharmacy (Bhagavathula et al., 2022; Jungo et al., 2021; Alhawassi et al., 2019; Magalhães et al., 2019; Hill-Taylor et al., 2016). Multimorbidity, defined as the presence of

two or more chronic diseases in geriatric patients, affects up to 67% of the elderly population (Salive, 2013). An Indonesian study (Abdulah et al., 2018) identified polypharmacy, defined as the concurrent use of five or more drugs in patients or prescriptions (Kojima, 2018), as a significant factor associated with PIMs (odds ratio (OR) 1.2). Polypharmacy can also increase the risk of frailty by causing ADR; therefore, regular reviews of prescriptions and medications for geriatric patients are essential to prevent harm (Kojima, 2018).

Explicit tools can simplify the medication review process by alerting prescribers to PIMs in geriatric prescriptions (Curtin et al., 2019). Studies have utilized various tools to identify PIMs in hospitalized elderly patients, with the Beers criteria and the STOPP/START tool being the most frequently used (Alshammari et al., 2021). Implementing explicit criteria in the prescribing process has been associated with a reduction in potential prescribing omissions (PPOs) (Atmaja et al., 2022), an increase in potentially avoidable ADRs (Hill-Taylor et al., 2016), and more favourable clinical or non-clinical outcomes in no-PIMs geriatric patients (Alshammari et al., 2021). However, information on the prevalence of PIMs among Indonesian geriatric patients is scarce (Abdulah et al., 2018), particularly in hospital outpatients. Previous studies have focused on specific wards or polyclinics, such as internal medicine (Nurmainah & Astuti, 2022) and cardiovascular clinics (Wulansari et al., 2023), or assessed PIMs among inpatients. Consequently, this study aimed to evaluate the patterns of Potentially Inappropriate Medications (PIMs) among geriatric outpatients in Yogyakarta, Indonesia. The investigation focused on determining the prevalence of PIMs, identifying the specific pharmacological agents involved, and analyzing associated risk factors. These factors included polypharmacy, multimorbidity, female gender, employment status, and health insurance coverage, specifically among patients aged 60 years and older.

MATERIAL AND METHODS

Study Design

We conducted this study at two teaching hospitals in Yogyakarta, Indonesia, using a retrospective observational design. We collected the data from the medical records of patients under 60 years old from August to October 2022. The Medical and Health Research Ethics Committee,

Faculty of Medicine, Public Health, and Nursing, Gadjah Mada University—Dr. Sardjito General Hospital granted approval for this study under reference number KE/FK/1375/EC/2022.

Subject of the Study

The total number of geriatric outpatients in Hospital A was 2,374 per month, while in Hospital B, it was 941 per month. Lemeshow et al. (1990) introduced a formula for calculating the minimum sample size.

$$n = \frac{Z_{\alpha/2}^2 P \times (1 - P) N}{d^2 (N - 1) + Z_{\alpha/2}^2 P \times (1 - P)}$$

We used a 95% confidence interval (CI) and the 52% prevalence of PIMs from a previous study in Karawang, Indonesia, which included 3,315 patients. We determined the required minimum sample size to be 344 patients. We added 10% to ensure an adequate sample size, resulting in a minimum of 379 patients. The inclusion criteria comprised: 1) patients who were 60 years of age or older, 2) attended an outpatient clinic, and 3) were prescribed medications by physicians. Exclusion criteria included: 1) patients who were prescribed only non-oral drugs; and 2) patients whose data were without serum creatinine data or estimated creatinine clearance data, even if diagnosed with chronic kidney disease (CKD). We used a stratified random sampling method to select the study subjects. We received 281 patients from Hospital A and 112 patients from Hospital B. We collected and coded data on demographic characteristics, prescription medications (including names, doses, frequency, and total number of drugs dispensed), and diagnoses (primary, secondary, and historical) to safeguard the patients' identities.

Outcome of the Study

The study's main outcome was the prevalence of PIMs. The criteria used for evaluating PIMs from prescriptions were the AGS Beers® Criteria 2019 (American Geriatrics Society, 2019) and the STOPP_INA tool (Fauziyah et al., 2020), which was based on the STOPP/START version 2 tool (O'Mahony et al., 2014). We summarized the PIMs assessment in our study population based on the two explicit criteria used in a tabular format. Percentages were calculated based on total PIMs, total prescriptions containing PIMs, and drugs causing PIMs. The secondary outcome focused on factors associated with the occurrence of PIMs in geriatric patients. We examined multimorbidity,

polypharmacy, age, sex, working status, and health insurance as factors that precipitated PIMs in geriatric patients. Salive (2013) defined multimorbidity as the presence of two or more chronic diseases in geriatric patients. Polypharmacy was defined as the use of five or more medications in one prescription (Kojima, 2018). Patients' ages were classified as 60 to 74 years old or ≥ 75 years old, while working status and health insurance were classified as yes or no.

Data Analysis

PIMs were identified using the Beers Criteria and STOPP_INA, with data reported in two units: patients and PIM cases. A 'patient' was counted if at least one medication in their prescription met the PIM criteria, whereas a 'PIM case' referred to each specific instance of a PIM-categorized drug identified. We used Chi-square tests to analyze demographic characteristics and identify differences between the PIMs and the no-PIMs groups. We assessed all variables, including multimorbidity, polypharmacy, age, sex, working status, and health insurance, for their potential as covariates using a logistic regression model.

RESULTS AND DISCUSSION

This study included 393 subjects (Table 1). Respondents were diagnosed with a variety of chronic diseases. Type 2 diabetes mellitus, congestive heart failure, non-hemorrhagic stroke, liver cirrhosis, and ischemic heart disease were the top 5 chronic diseases experienced by respondents in this study. Predominantly, respondents displayed either no multimorbidity or less than 2 diagnosed chronic diseases (276 respondents, 70.2%). The range of multimorbidity experienced by respondents ranged from two to five chronic diseases, with a significant difference in the proportion with multimorbidity between the PIMs group (46.7%) and the no PIMs group (20.9%). In the present study, we observed that multimorbidity occurred in 29.8% of geriatric patients, lower than that reported in a previous study based on data from the national life survey in Indonesia, which found a prevalence of multimorbidity of 35.7% in adults aged 40 years and above (Hussain et al., 2015).

Respondents' polypharmacy prevalence ranged from 5 drugs to 13 drugs per prescription. The PIMs group had a higher overall percentage of respondents experiencing polypharmacy (77%) than the no PIMs group (24%), with statistically significant differences between the groups. The

overall rate of polypharmacy in our study population was 42.2%, which is higher than the rates reported in China (23%) and Ethiopia (33%), but lower than the rates reported in a previous study in the emergency room of a national central hospital in Jakarta, Indonesia (57.6%) or in a hospital in Saudi Arabia (65.3%) (Bhagavathula et al., 2022; Tian et al., 2022; Soejono & Rizka, 2021; Meraya et al., 2020). In the past two decades, there has been a notable rise in comorbidities among geriatric patients, paralleled by an escalation in prescribed medications, commonly referred to as polypharmacy (Reimers et al., 2018). Researchers have correlated an increased occurrence of PIMs with a higher frequency of prescribed drugs (Achterhof et al., 2020).

The mean age of respondents was 68.54 ± 6.461 years, with the oldest respondent being 86 years. In this study, the proportion of female elderly respondents surpasses that of male respondents, which is consistent with previous research in Yogyakarta, where the majority of geriatric patients were female (Rahmawati et al., 2019). In contrast, a higher proportion of male respondents experienced PIMs compared to female respondents, with percentages of 59.3% and 48.8%, respectively, and this difference between the groups was statistically significant. The majority of respondents were still working, both in the PIMs group (63.7%) and the non-PIMs group (67.4%), and there were no significant differences in working status between groups. The majority of respondents enrolled in health insurance, with only 14.8% in the PIMs group and 19.8% in the no PIMs group not using health insurance. However, we observed no significant differences between the groups in this regard.

Various explicit criteria can evaluate PIMs in geriatric patients, with the Beers Criteria and STOPP/START Tool being the most widely used in clinical practice (Alshammari et al., 2021). Beers criteria, characterized by their conciseness and informed by extensive evidence review and a robust grading methodology, offer a comprehensive list of standard drugs and drug classes in the USA. On the other hand, the STOPP/START tool, which has strong randomized controlled trial (RCT) evidence of clinical benefit, is used to lower PIMs and includes drugs that are sold in Europe (Curtin et al., 2019). Indonesia translated the STOP/START tool into STOPP_INA and subsequently validated it. Internal consistency assessments yielded satisfactory results (Chang et al., 2023; Fauziyah et al., 2020).

Table I. Characteristics of Subjects and PIMs Prevalence

Characteristics	Overall (N=393) n(%)	No PIMs (N=258) n(%)	PIMs (N=135) n(%)	p-value
<i>Multimorbidity</i>				0.001*
No Multimorbidity (0-1 disease)	276 (70.2%)	204 (79.1%)	72 (53.3%)	
Multimorbidity (2 disease)	73 (18.6%)	36 (14.0%)	37 (27.4%)	
Multimorbidity (3 disease)	29 (7.4%)	12 (4.7%)	17 (12.6%)	
Multimorbidity (4 disease)	13 (3.3%)	6 (2.3%)	7 (5.2%)	
Multimorbidity (5 disease)	2 (0.5%)	0 (0.0%)	2 (1.5%)	
<i>Polypharmacy</i>				0.000*
No Polypharmacy (1-4 drugs)	227 (57.8%)	196 (76.0%)	31 (23.0%)	
Polypharmacy (5 drugs or more)	166 (42.2%)	62 (24.0%)	104(77.0%)	
<i>Age</i>				0.157
Mean ± SD		68.54 ± 6.461		
60-74 years	318 (80.9%)	213 (82.6%)	105 (77.8%)	
≥ 75 years	75 (19.1%)	45 (17.4%)	30 (22.2%)	
<i>Sex</i>				0.049*
Female	187 (47,6%)	132 (51.2%)	55 (40.7%)	
Male	206 (52,4%)	126 (48.8%)	80 (59.3%)	
<i>Working status</i>				0.457
No	133 (33.8%)	84 (32.6%)	49 (36.3%)	
Yes	260 (66.2%)	174 (67.4%)	86 (63.7%)	
<i>Health Insurance</i>				0.226
No	71 (18.1%)	51 (19.8%)	20 (14.8%)	
Yes	322 (81.9%)	207 (80.2%)	115 (85.2%)	

*Statistically significant (p<0.05) analyzed using Chi-square test; SD: standard deviation; PIMs potentially inappropriate medications

Table II. Prevalence of PIMs Detected by Certain Explicit Criteria

Amount of PIMs/ prescription	Total PIMs		Beers Criteria 2019		STOPP_INA	
	Number of Patients	Number of Cases	Number of Patients	Number of Cases	Number of Patients	Number of Cases
1 PIMs	89	89	44	44	79	79
2 PIMs	36	72	7	14	25	50
3 PIMs	8	24	3	9	4	12
4 PIMs	2	8	0	0	0	0
Total	135	193	54	67	108	141

The integration of Beers Criteria (2019) and STOPP_INA as complementary assessment tools identified 193 total PIM cases across 135 patients (34.35% of the study population). In this context, a 'patient' represents an individual with at least one PIM in their prescription, while 'PIM cases' refers to the total frequency of specific PIM-categorized drugs detected. Evaluation using STOPP_INA yielded a higher number of occurrences (n=141)

compared to the Beers Criteria (n=67). This dual-criteria approach resulted in a higher total count than either tool alone, as several PIM instances were uniquely identified by only one of the criteria (Table II). The total number of drugs implicated in PIMs in geriatric patients is categorized into 19 different drug classes (Table III). The prevalence of PIMs assessed by the STOPP_INA tool and Beers' Criteria 2019 among geriatric outpatients in the

study location was found to be 27.5% and 13.7%, respectively, which was quite similar to a previous study in tertiary care hospitals in India, which reported a 26% prevalence of PIMs (Sheth et al., 2020). Notably, the explicit criteria used for medication appropriateness assessment influence the prevalence of PIMs, which can vary across countries. For instance, reports from other Asian countries indicate that the prevalence of PIMs is 47.51% in primary care in Hong Kong, 62.6% in outpatient clinics in Qatar hospitals, and 47.9% in hospitalized elderly in Japan (Zhang et al., 2021; Alyazeedi et al., 2019; Komagamine, 2018). Using the Beers Criteria and the STOPP/START tool as clear criteria for evaluation has been linked to more PIMs being found in prescriptions than the PRISCUS list. This was shown by a study in Spain, where the prevalence of PIMs was 90.8%, 96.3%, and 35.3%, respectively (Díez et al., 2022). In line with what was found in Poland, this study found that the STOPP_INA tool found more PIMs than the 2019 Beers' Criteria (Lisowska et al., 2022). This is different from what was found in Portugal, where the 2019 Beers' Criteria found more PIMs than the STOPP/START version 2 (Perpétuo et al., 2021).

Based on the STOPP_INA tool, the primary drug classes associated with PIMs in this study were aspirin, diuretics, and angiotensin receptor blockers (ARBs). In contrast, the 2019 Beers Criteria identified benzodiazepines, non-steroidal anti-inflammatory drugs (NSAIDs), and aspirin as the top three contributors. These findings are consistent with a previous study in Jakarta, which reported that furosemide and spironolactone were the most frequent PIMs identified by the Beers Criteria, while aspirin or clopidogrel usage predominated in PIMs identified via STOPP criteria (Viviandhari et al., 2022). Studies conducted in China and Japan have implicated benzodiazepines as a cause of PIMs (Komagamine, 2018; Ma et al., 2018). Furthermore, a prior study in primary care in Indonesia identified antihistamines and NSAIDs as the top two drugs contributing to PIMs among the elderly, a finding consistent with the results of this study (Abdulah et al., 2018).

Aspirin emerged as a primary contributor to PIMs in this study, particularly when assessed through the STOPP_INA tool, and was also ranked among the top three PIM causes according to the 2019 Beers Criteria. Based on the STOPP_INA criteria, aspirin was identified as potentially inappropriate primarily due to its use in combination with clopidogrel for primary stroke

prevention and its administration without a proton pump inhibitor (PPI) for gastrointestinal protection (Fauziyah et al., 2020).

The identification of aspirin as a PIM is further supported by clinical evidence regarding its risk-benefit profile in geriatric patients. While aspirin is frequently prescribed for stroke, acute coronary syndrome (ACS), and post-percutaneous coronary intervention (PCI), its use in patients with heart failure may exacerbate fluid retention (American Geriatrics Society, 2019). Recent meta-analyses have evaluated the efficacy and safety profiles of antiplatelet therapies, particularly the combination of aspirin and clopidogrel. Hao et al. (2018) demonstrated that clopidogrel administered for less than 21 days in ischemic stroke cases offered superior safety compared to aspirin monotherapy, despite a marginal 0.2% increase in intracranial hemorrhage risk. Correspondingly, while low-dose aspirin is strongly evidenced to reduce bleeding risks, it exhibits lower efficacy compared to alternative antiplatelet agents in patients with established cardiovascular disease (CVD) or those at high cardiovascular risk (Veronese et al., 2020). Furthermore, current systematic evidence suggests that cilostazol represents a safer therapeutic alternative for ischemic stroke patients than low-to-medium-dose aspirin (Jung et al., 2022).

Long-term aspirin therapy necessitates gastroprotection, such as the use of PPIs, to mitigate the risk of gastrointestinal bleeding (Fauziyah et al., 2020). However, the prolonged use of PPIs remains a clinical concern due to potential complications, including enteric infections, community-acquired pneumonia, vitamin B12 deficiency, and an elevated risk of kidney disease (Haastrup et al., 2018). Furthermore, PPI utilization has been associated with increased fracture risks and impaired magnesium absorption, both of which are particularly problematic for the elderly population (Castellana et al., 2021). Consequently, PPI therapy should be guided by clear indications and a well-defined, time-limited prescription endpoint to ensure patient safety (Jaynes & Kumar, 2019).

The concurrent use of spironolactone and candesartan carries significant pharmacological implications, particularly an elevated risk of hyperkalemia in the elderly (Fauziyah et al., 2020). As an aldosterone antagonist, spironolactone inhibits potassium ion (K⁺) excretion in the distal renal tubules.

Table III. Percentage of PIMs and Underlying Reason

Drug Class	Drug Name	Reason Based on STOPP_INA (number of cases)	Total number of cases (%)	Reason Based on Beers' Criteria 2019 (number of cases)	Total number of cases (%)
Antiplatelet	Aspirin	Combined with clopidogrel for primary stroke prevention (11) Unaccompanied by proton-pump inhibitor (53)	64 (45,4%)	Used in patient with heart failure (8)	8 (11.9%)
Benzodiazepine	Diazepam Lorazepam Clonazepam Alprazolam	Duration of use >4 weeks (2) Duration of use >4 weeks (2) Use as sedative (1)	5 (3,5%)	Increased sensitivity and decreased metabolism (7) increased sensitivity to benzodiazepines (4) Increased sensitivity and decreased metabolism (1) increased sensitivity to benzodiazepines (2)	14 (20.9%)
Non-Steroid Anti-Inflammatory Drugs	Sodium Diclofenac Meloxicam Mefenamic Acid Ibuprofen Ketorolac	Duplication to paracetamol use in patients with OA (2)	2 (1,4%)	Antiplatelet use (clostazol) (1); Age >75 years (1); Used in CHF patient (1) Antiplatelet use (aspirin) (1); Used in CHF patients (1) Antiplatelet use (cilostazol) (1); Age >75 years (3) Used in low-risk patient but without gastroprotection (1) Increased risk of gastrointestinal bleeding/peptic ulcer disease and acute kidney injury (1)	11 (16.4%)
Atypical Antipsychotic	Clozapine Sulpiride Trifluoperazine	High Risk of Fall (1)	1 (0,7%)	Used in non-schizophrenia/ bipolar disorder/ chemotherapy antiemetic patients (2) Used in non-schizophrenia/ bipolar disorder/ chemotherapy antiemetic patients (2) Used in non-schizophrenia/ bipolar disorder/ chemotherapy antiemetic patients (1)	5 (7.5%)
Typical Antipsychotic	Haloperidol	High Risk of Fall (1)	1 (0,7%)	Used in non-schizophrenia/ bipolar disorder/ chemotherapy antiemetic patients (1)	2 (2.9%)
Antidiabetic	Metformin Glimepiride	Creatinine Clearance <30 ml/min (1)	1 (0,7%)	higher risk of severe prolonged hypoglycemia in older adults (5)	5 (7.5%)
Tricyclic Antidepressant	Amitriptyline	High risk of adverse drug reaction (2); history of chronic heart failure (1); history of prostate disorder (1)	4 (2,8%)	Highly anticholinergic, sedating, and cause orthostatic hypotension (4)	4 (5.9%)
Corticosteroid	Methylprednisolone	Duration of use > three months (2)	2 (1,4%)	Potential drug interaction: combination with NSAID (aspirin 1) (diclofenac sodium 2) (meloxicam 1)	4 (5.9%)

mcg : microgram(s); LVEF: Left Ventricular Ejection Fraction; OA: Osteoarthritis; CHF: Congestive Heart Failure; NSAIDs: Non Steroidal Anti Inflammatory Drugs

Table III. Continued

Drug Class	Drug Name	Reason Based on STOPP_INA (number of cases)	Total number of cases (%)	Reason Based on Beers' Criteria 2019 (number of cases)	Total number of cases (%)
Antihistamine	Cetirizine	Duplication of antihistamine (1); Age > 70 years (1)	4 (2,8%)		
	Loratadine	Duplication of antihistamine (1)		Highly anticholinergic; clearance reduced, and tolerance develops; Risk of adverse effect (2)	4 (5.9%)
	Chlorpheniramine Maleate	Age > 70 years (1)		Highly anticholinergic; clearance reduced, and tolerance develops; Risk of adverse effect (2)	
	Triprolidine			Used over 8 weeks in non-high-risk patients (2)	3 (4.6%)
Proton Pump Inhibitors	Lansoprazole	Duration of use > eight weeks (8)	9 (6,4%)	Used over 8 weeks in non-high-risk patients (1)	1 (1.5%)
	Omeprazole	Duration of use > 8 weeks (1)		Used in patient with primary hypertension (1)	
Central Antihypertensive	Clonidine	Age > 70 years (1)	1 (0,7%)		
Positive Inotropic	Digoxin	Dose > 125 mcg/day (1); Use in normal LVEF patient with heart failure (1)	2 (1,4%)	Used in CHF patient (1)	1 (1.5%)
Diuretic	Spirolactone	Using angiotensin receptor blockers (19)	21 (14,9%)		
	Furosemide	Use as antihypertensive (1)			
	Hydrochlorothiazide	Presence of hyperuricemia (1)			
Angiotensin Receptor Blockers	Candesartan	Using spironolactone (15)	19 (13,5%)		
	Valsartan	Using spironolactone (3)			
	Irbesartan	Using spironolactone (1)			
Calcium Channel Blockers	Amlodipine	History of Parkinson syndrome (1)	4 (2,8%)		
	Diltiazem	Using beta-blocker (3)			
Anti Gout/Hyperuricemia	Colchicine	Duration of use > 3 months (1)	1 (0,7%)		
Antimuscarinic	Trihexyphenidyl			Not recommended for prevention or treatment of extrapyramidal symptoms with antipsychotics (3)	3 (4.6%)
Opioid	morphine			Potential drug interaction with gabapentin: increased risk of adverse events (1)	1 (1.5%)
Anticoagulant	rivaroxaban			Used in patient with creatinine clearance <50 ml/min (1)	1 (1.5%)
	Total PIM (by items)		141		67

mcg : microgram(s); LVEF: Left Ventricular Ejection Fraction; OA: Osteoarthritis; CHF: Congestive Heart Failure; NSAIDs: Non Steroidal Anti Inflammatory Drugs

Table IV. Factors Related to PIMs Occurrence

Variables	p-value	OR	B	CI (95%)
Multimorbidity	0.103	/	0.218	0.957 – 1.1617
Polypharmacy	0.000*	/	0.567	1.526 – 2.036
Age	0.540	/	0.012	0.973 – 1.053
Male Sex	0.054	1.647	/	0.991 – 2.736
Working	0.722	0.908	/	0.532 – 1.548
Health Insurance	0.253	0.682	/	0.354 – 1.313

*Statistically significant (p<0.05) tested using logistic regression test; OR: odds ratio for categorical variables; B: regression coefficient for numerical variables; CI: Confidence Interval

While the combination of spironolactone and candesartan may reduce proteinuria in patients with chronic kidney disease (CKD), it necessitates rigorous monitoring (Erraez et al., 2021). Although some meta-analyses report a modest mean increase in serum potassium (<0.20 mEq/L), the clinical concern lies in the significantly higher risk of severe hyperkalemia and related hospitalizations among vulnerable populations, such as those with impaired renal function (Villa-Zapata et al., 2021). There is only a small amount of recent literature on the concurrent use of candesartan and spironolactone. A 2007 randomized controlled trial (RCT) provided the sole evidence suggesting that ARBs could provide additional therapeutic benefits to heart failure patients already on spironolactone. Notably, patients receiving spironolactone at baseline did not have an elevated relative risk of discontinuing candesartan due to hyperkalemia (Weir et al., 2008).

Research has linked the use of benzodiazepines among the elderly to cognitive impairment and an increased risk of falls (Liu et al., 2020; Masudo et al., 2019). Despite this, physicians frequently prescribe benzodiazepines to elderly individuals suffering from insomnia, a condition common in this demographic, due to their effective enhancement of total sleep time and quality (Samara et al., 2020). Moreover, benzodiazepines are often administered to patients experiencing pain, particularly those with chronic pain accompanied by symptoms of stress, anxiety, fearfulness, and disrupted sleep patterns. However, because of their adverse effects, doctors typically limit the use of benzodiazepines to a four-week duration (Pergolizzi & LeQuang, 2020). Pain management favors diazepam, a commonly used benzodiazepine, for its muscle relaxant properties and efficacy in treating spasms. This study found

diazepam associated with lumbar pain in patients, prescribing it in combination with another analgesic in a low-dose regimen. Nevertheless, older adults exhibit heightened sensitivity to benzodiazepines and metabolize long-acting agents at a slower rate, necessitating cautious prescription practices (Witenko et al., 2014). This study identified other benzodiazepines like lorazepam, clonazepam, and alprazolam as PIMs due to their use in the elderly population, in addition to diazepam (American Geriatrics Society, 2019). Researchers have linked chronic benzodiazepine use to various adverse effects, including the impairment of intellectual and cognitive functions in the elderly (Louvet et al., 2015). A previous Canadian study found a significant excess risk of hip fractures, hospitalizations, long-term care admissions, and mortality among elderly individuals who received chronic benzodiazepine prescriptions (Davies et al., 2022).

The American Geriatrics Society (2019) has identified NSAIDs use as a PIMs in geriatric patients, particularly those in high-risk categories such as individuals over 75 years of age or those concurrently taking corticosteroids, anticoagulants, or antiplatelet agents. In our study, we observed that 16.4% of instances of PIMs, as determined by Beers' Criteria 2019, were attributable to NSAIDs use in high-risk patients, such as those aged over 75 years and those concurrently receiving antiplatelet therapy. Notably, a previous review on NSAIDs showed that aging can raise the risk of gastrointestinal bleeding. NSAIDs make this risk worse by stopping the production of prostaglandins, which weakens the protective gastrointestinal mucosal barrier and makes bleeding more likely (Wongrakpanich et al., 2018). In Portugal, a pharmacovigilance study found that the geriatric population's use of NSAIDs

was associated with an increased risk of adverse events, and the consistent prescription of gastroprotective agents did not accompany NSAIDs. This study highlights the significance of assessing renal function in elderly individuals 75 years or older who receive NSAIDs prescriptions, given the observed increased risk of acute kidney failure in this demographic (Monteiro et al., 2022).

The study of determinants influencing PIMs occurrence was varied; most of the studies agreed that polypharmacy and multimorbidity were strong determinants of PIMs in the elderly (Abdulah et al., 2018; Almeida et al., 2019; Chen & Zhang, 2021; Zhang et al., 2021). Other studies suggest that sex, age, and other patient characteristics are factors related to PIMs in the elderly (Zhang et al., 2021; Almeida et al., 2019; Miller et al., 2017;). In this study, we examined six factors potentially associated with PIMs occurrences: polypharmacy, multimorbidity, age, sex, working status, and health insurance. In the multivariate analysis, only polypharmacy demonstrated a significant correlation with PIMs occurrences ($p < 0.05$), as shown in Table IV. Previous research in two hospitals in Jakarta, Indonesia, similarly identified polypharmacy as an independent predictor of PIMs occurrences (Viviandhari et al., 2020), aligning with this finding. Indeed, several studies have consistently highlighted polypharmacy as a predictive factor correlated with PIMs occurrences, although other predictors have also been identified in some instances (Chen & Zhang, 2021; Zhang et al., 2021; Almeida et al., 2019; Abdulah et al., 2018; Oliveira et al., 2015). Interestingly, our study did not observe significant correlations with certain predictors that previous studies found to correlate significantly with PIMs, such as male sex in a US study (Miller et al., 2017) or female sex in a Hong Kong study (Zhang et al., 2021). Moreover, while some studies suggest that PIMs occurrence is lower in individuals aged ≥ 75 years compared to those aged 60-74 or under 70 years (Bhagavathula et al., 2022; Almeida et al., 2019; Miller et al., 2017), our study did not observe a significant correlation between PIMs occurrence and age. These inconsistent results might depend on the amount and proportion of study subjects. Therefore, further evidence is required to determine the relationship between sex, age, and the occurrence of PIMs (San-José et al., 2015). Similarly, a study involving geriatric patients admitted to a Spanish hospital revealed multimorbidity as a strong predictor of PIMs (Bhagavathula et al., 2022).

The limitations of this study include its retrospective design, which relies on the accuracy and completeness of medical records and may lack clinical context for specific prescribing decisions. Furthermore, the use of explicit criteria (Beers and STOPP/START), while evidence-based and widely used in Indonesia, is inherently criterion-based rather than judgment-based. Consequently, some medications intended for unique circumstances, such as last-resort therapies or constraints due to insurance restrictions, might have been classified as potentially inappropriate. Additionally, this research primarily focused on patient-related factors, without correlating other variables, such as prescriber-related factors. Therefore, further research is warranted to delve deeper into these issues and to provide a more comprehensive understanding of PIM determinants in geriatric care.

CONCLUSION

In conclusion, this study found a relatively low prevalence of PIMs (34.35%) among the geriatric population observed. Polypharmacy emerged as a robust predictor of PIM occurrences, with aspirin ranking among the top three drug classes contributing to PIMs under both Beers' and STOPP_INA criteria. These findings underscore the need for stringent monitoring and meticulous drug selection to mitigate potential harm. Given the potential association between multimorbidity and polypharmacy in geriatric patients, clinicians must prioritize medication safety to improve health outcomes.

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CONFLICT OF INTEREST

All authors declared the absence of any potential conflicts of interest pertinent to this article.

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